REMARKS

Favorable reconsideration is respectfully requested in view of the following remarks.

I. CLAIM STATUS

Claims 26, 29-30, 32, 35-43 and 48-51 are pending in the application and stand rejected.

Applicants thank the Examiner for the careful examination of this case and respectfully request reexamination and reconsideration of the case. Below Applicants address the rejections in the Office Action and explain why the rejections are not applicable to the pending claims.

This amendment must be entered and considered after final rejection, as the claims have not been amended by this response. Therefore, there is nothing that would require further consideration and/or search, and hence no ground for refusing entry to this amendment. Accordingly, if the next Office Action on the merits includes a new rejection of one or more claims, the Action must be non-final.

II. OBVIOUSNESS REJECTION

Claims 26, 29-30, 32, 35-43 and 48-51 were newly rejected under 35 U.S.C. § 103(a) as allegedly obvious over POWELL et al. (Molecular Breeding, vol. 2, pp. 225-238, 1996) in

view of THOMANN et al. (WO 01/53529 A2, published July 26, 2001) for the reasons in item 17 on pages 6-10 of the Office Action.

This rejection is respectfully traversed.

It is well established that to support a *prima facie* case of obviousness, the Office must provide a rationale showing that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions to yield predictable results. *See, KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 U.S.P.Q.2d 1385, 1395 (2007); and M.P.E.P., Eighth Ed., Rev. 6 (September 2007) at § 2143.02.

In the instant case, independent claim 26, as amended per the response filed November 26, 2007, recites:

> 26. A method for analyzing or amplifying a nucleic acid sequence, comprising analyzing or amplifying a nucleic acid with an S3P primer, comprising at least part of a consensus sequence of a splice-site border sequence, and at least one AFLP primer which contains at least one selective nucleotide at its 3' end, wherein the nucleic acid sequence comprises a restriction fragment with one oligonucleotide adapter at both ends and wherein said restriction fragment is derived from genomic DNA, mitochondrial DNA, chloroplast DNA, or recombinant DNA.

Note that independent claims 41-43 also require the use of one or more S3P primers. As such, the independent claims of the instant application all require use of an S3P primer.

Applicants respectfully submit that POWELL and THOMANN, taken alone or in combination, do not teach, suggest or make obvious the use of an S3P primer as in the method of independent claims 26 and 41-43.

POWELL compared the utility of RFLP, RAPD, AFLP and SSR markers in soybean germplasm analysis. As such, the document seems rather irrelevant for the present application, which is directed to methods for analyzing or amplifying a nucleic acid sequence. Further, POWELL fails to disclose or suggest the use of an S3P primer as required in independent claims 26 and 41-43. Indeed, the Examiner acknowledges such at page 7, lines 16-18 of the Office Action.

Instead, at page 7, lines 20-23 of the Office Action, the Examiner states that THOMANN allegedly discloses "analyzing or amplifying a nucleic acid with an S3P primer, comprising at least part of a consensus sequence of a splice-site border sequence." Applicants respectfully disagree and submit that the Office does not fully understand the teachings in THOMANN, and is thus wrong in the obviousness assessment.

THOMANN is concerned with rapid determination of gene structure using a known cDNA sequence. For a cDNA or EST sequence, it is known that not all sequence information pertinent to gene structure and phenotypic variation is available. A highly relevant portion of a gene can be identified that may contain gene structure information or phenotypic allelic variation

information. One such highly relevant portion of a gene is that portion of the intron that encompasses the consensus splice sequence (see page 4, lines 8-12 of THOMANN). That sequence is not known with the cDNA sequence, because the cDNA sequence does not contain intron sequences. Thus, in order to determine important intron sequences of a gene to a known cDNA sequence, primer pairs are used in such a way that they would amplify the entire cDNA sequence.

However, instead of using cDNA as a template, genomic DNA (*e.g.*, as present in BAC DNA) is used as a template. If the 2 primers in a primer pair are located each on a different side of an intron sequence, an amplicon will be obtained that is much larger than one would expect based on the known cDNA sequence. Such amplicon then contains intron sequences.

In view of such understanding, Applicants respectfully submit that THOMANN does not disclose or suggest the use of an S3P primer, *i.e.*, a primer that contains both exon and intron sequence, to amplify a portion of the gene to a known cDNA sequence as required in claims 26 and 41-43. Indeed, THOMANN does not even know the intron sequence, as the aim of the method in THOMANN is to determine such intron sequence.

By contrast, the S3P primer of the instant claims contains sequences complementary to both intron and exon sequences. In this regard, please see page 9, lines 4-11 of the disclosure of the instant application, wherein the S3P-primer is

defined as:

> As also schematically shown in Figure 1, the S3P-primer (1) may be considered to comprise essentially two parts, i.e. a 3'-part and a 5'-part, indicated in Figure 1 as (4) and (5), respectively. Part of the 3'part (4) of the S3P-primer (1) is (intended to be) essentially complementary to (part of the sequence of) the **intron (3A)**, more in particular to part of the consensus sequence of the intron section. The 5'-part (5) of the S3P-primer (1) is (intended to be) complementary to the exon, more in particular to the consensus sequence of the **exon sequence (3B)**. [Emphasis added.]

Thus, the primer in THOMANN is not the same as the S3P primer of the claims. This position is further supported by the evidence in Tables V and VIII (pages 17 and 25, respectively) in THOMANN as discussed below.

On Table V and page 17, lines 16-17, THOMANN states that "Primer 6 and 8 hybridized at an intron/exon boundary and are therefore not expected to result in a successful sequencing reaction." However, primers 6 and 8 were generated using p53 cDNA (see page 16, lines 1-2 of THOMANN), *i.e.*, a DNA sequence not containing intron sequences. The only possible conclusion can be that primers 6 and 8 were located at the position where an intron was excised, *i.e.*, containing sequences from 2 different exons. This is consistent with the statement in THOMANN that these primers were not expected to result in a successful sequencing reaction. Indeed, the two different exons are separated in the gene structure by an intron, and as such, primers 6 and 8 will no longer hybridize to yield an amplicon. Thus, primers 6 and 8 in

THOMANN did not actually contain both exon and intron sequences and are therefore not S3P primers as required in claims 26 and 41-43 of the present application.

As further support, please Table VIII of THOMANN, wherein primers 947L and 950U were designed from CYP450 2C19 cDNA, which is a DNA sequence not containing intron sequences (see page 25, lines 27-29). As such, it is believed that these primers in THOMANN will also not contain any portion of an intron sequence, but instead were located at the position were an intron was excised, *i.e.*, containing sequences from two different exons. See also the comment made in the appendix to Table VIII (page 27, lines 22-23) noting that primers 947L and 950U hybridized to an exon - intron boundary, and thus did not yield any sequence. This comment is consistent with the idea that the primers in THOMANN contain sequences from two different exons, which are separated in the gene structure by an intron and inability to hybridize to the gene structure. Thus, the primers in THOMANN will not hybridize to the gene structure template and a sequence will not be obtained.

In contrast, if the above primers in THOMANN were actually S3P primers as required in the instant claims, an amplicon would for sure be expected on the gene structure (containing both exon and intron sequence). The fact that no sequences were obtained strengthens the above conclusion that the

primers in THOMANN do not contain both exon and intron sequences, and thus are not the S3P primer of the instant claims.

In view of the above, it is clear that the primers in THOMANN differ structurally and functionally from the S3P primer of the current claims.

Also, give the above discussed difficulties in the primer of THOMANN, Applicants further submit that the combination of POWELL and THOMANN would fail to yield predictable results as such a combination would not arrive at the claimed method.

Thus, in contrast to the Office's position, THOMANN cannot be relied upon as disclosing the S3P primer of independent claims 26 and 41-43. For these reasons, Applicants respectfully submit that the combination of POWELL and THOMANN fails to disclose or suggest each and every element of independent claims 26 and 41-43 and fails to yield predictable results. Therefore, the combination of POWELL and THOMANN cannot render obvious the method of independent claims 26 and 41-43.

Thus, independent claims 26 and 41-43 are novel and unobvious over the combination of POWELL and THOMANN.

Claims 29, 30, 32, 35-40 and 48-51 depend, either directly or indirectly, on either claim 26, 41, 42 or 43. These dependent claims are also novel and unobvious over the cited references for the same reasons set forth above due to their dependency on the above-discussed independent claims.

Therefore, Applicants respectfully submit that the above-noted 103(a) obviousness rejection is untenable and should be withdrawn.

III. CONCLUSION

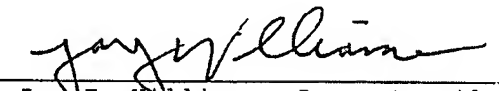
In view of the foregoing remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON



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